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Evaluation of hematological parameters in the differentiation of bile reflux gastritis and *Helicobacter pylori* gastritis in children

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ABSTRACT

Aims: Endoscopy is used in the diagnosis of bile reflux gastritis and *Helicobacter pylori (H. pylori)* gastritis. However, endoscopy is an invasive procedure with complications. The study proposes that by analyzing the absolute neutrophil - lymphocyte count ratio and mean platelet volume, it might be possible to distinguish between *H. pylori* gastritis and bile reflux gastritis.

Methods: All patients with endoscopic and histopathological confirmation *H. pylori* gastritis of (Group 1), bile reflux gastritis (Group 2), or both (Group 3) were included in this retrospective study. White blood cells, absolute neutrophil count, absolute lymphocyte count and mean platelet volume were analyzed in all patients. The absolute neutrophil/lymphocyte ratio was calculated.

Results: 218 patients were included in the study. The median absolute neutrophil-lymphocyte ratio was 1.33 in *H. pylori* gastritis, 1.56 in bile reflux gastritis, and 1.47 in both. The mean value of mean platelet volume was 9.97±0.82 in *H. pylori* gastritis, 10.16±0.81 in bile reflux gastritis, and 10.06±0.88 in both. The absolute neutrophil/lymphocyte ratio and mean platelet volume did not differ significantly between the groups.

Conclusion: According to our results, absolute neutrophil/lymphocyte ratio cannot be used as a differential diagnosis marker in children with *H. pylori* gastritis and bile reflux gastritis.

Keywords: Bile reflux gastritis, children, *Helicobacter pylori* gastritis, hematological

INTRODUCTION

Dyspepsia is characterized by various symptoms such as abdominal pain, discomfort in the epigastrium region (upper abdomen), nausea, loss of appetite, weight loss, heartburn, and regurgitation.[1] It's important to note that while the underlying cause of dyspepsia is often functional which there's no apparent structural abnormality, it can also be linked to organic, systemic, or metabolic diseases in some cases.[1-3] In the pediatric population, functional dyspepsia is more common than organic dyspepsia. Organic causes include *H. pylori* gastritis and bile reflux gastritis.[4,5] *H. pylori* is a type of bacteria that commonly infects the stomach. It is known to cause a local inflammatory response in the stomach mucosa, which can lead to gastritis and potentially peptic ulcers. The infection triggers an immune response in the body, leading to the activation of both innate and adaptive immune mechanisms. In particular, the T CD4+ cells are considered the main actors in the establishment of chronic inflammation. The innate immune response involves the activation of immune cells like neutrophils and macrophages, which attempt to eliminate the bacteria.[6] Bile reflux gastritis occurs when the contents of the duodenum, which can disrupt the gastric mucosal barrier with various factors, leak back into the stomach and cause inflammation.[7,8] The majority of cases involve asymptomatic chronic inflammation. Upper gastrointestinal endoscopy is used to differentiate between bile reflux gastritis and *H. pylori* gastritis. The ROMA IV criteria are used in the diagnosis of functional dyspepsia, a common gastrointestinal disorder characterized by recurring or chronic upper abdominal pain or discomfort.[9]

The absolute neutrophil-lymphocyte count ratio (ANC/ALC) is indeed considered to be a marker of subclinical inflammation in exacerbations of many lung diseases, obesity, and many heart diseases.[10,11] This can be an indication of an inflammatory response, as neutrophils are often recruited to sites of infection or inflammation.[12] Studies have indeed shown that elevated mean platelet volume (MPV) values can be associated with various conditions involving low-grade inflammation, such as diabetes and coronary artery disease.[13] The physiological response of circulating white blood cells (WBC) to stress, infection, or inflammation often leads to changes

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in the numbers of different types of leukocytes. This includes an increase in the number of neutrophils and a decrease in the number of lymphocytes. Due to these changes in leukocyte counts during times of stress or inflammation, the ANC/ALC ratio becomes a useful and sensitive marker for assessing the presence of inflammation. The absolute neutrophil-lymphocyte count ratio is derived from a hemogram test and is used as an inflammatory marker of various diseases. These ANC/ALC ratio and MPV in peripheral blood are used as parameters that provide information about the relationship between the inflammatory environment and physiological stress. In this study, our aim is to evaluate whether the hematological parameters are a guide in the differentiation of pediatric patients with bile reflux gastritis and *H. pylori* gastritis.

METHODS

The study was carried out with the permission of Sivas Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date:22.06.2022, Decision No: 2022-06/28). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

We conducted a retrospective study on 218 children who applied to Sivas Numune Hospital Pediatric Gastroenterology outpatient clinic with dyspeptic symptoms and underwent upper gastrointestinal endoscopy between January 2020 and July 2023. Gender, age, pathological data of endoscopy preparations and complete blood count data were analyzed. Patients with acute infection, chronic/previous (in the last 1 month) drug use, and chronic disease such as Celiac disease, inflammatory bowel disease, familial Mediterranean fever were not included the study.

The patients were divided into 3 groups according to the endoscopy and pathology results. Group 1 were those with *H. pylori* gastritis, Group 2 were those with bile reflux gastritis, and Group 3 were those with both. Sydney classification was used for data on the degree of chronic inflammation and *H. pylori* density.

In the hemogram parameters, WBC, ANC/ALC ratio, and MPV values were examined.

Statistical Analyses

All statistical analyzes were performed using the SPSS version 22.0 statistical software program (SPSS, Chicago, IL). Normality of distribution of numerical variables was evaluated. Numerical data were compared between groups using Kruskal-Wallis test (not normally distributed subjects) and One-Way ANOVA test (normally distributed subjects). Results were considered statistically significant when the P value was less than 0.05.

RESULTS

A total of 218 children were included in the study. Of the patients, 156 were girls and 62 were boys. The mean age of the patients was 14.47±3.07 years. Of the patients, 117 (53.7%) had *H. pylori* gastritis, 47 (21.5%) had bile reflux gastritis, 54 (24.8%) had both bile reflux gastritis and *H. pylori* gastritis.

When 171 patients with *H. pylori* gastritis were evaluated according to the degree of gastritis; *H. pylori* gastritis was mild in 110 patients, moderate in 26 patients, and severe in 35 patients.

Ulcers were detected in 27 (12.4%) patients, 9 of them (4.1%) in the stomach and 18 (8.3%) in the bulb.

The demographic characteristics, laboratory and endoscopic findings of the patients are summarized in **Table 1**.

Table 1. Demographic features, laboratory and endoscopic findings of the study group

n=218	(%)
Age (month) mean±SD	14.47±3.07
Gender	
Female	156 (71.6)
Male	62 (28.4)
Helicobacter pylori gastritis	117 (53.7)
Bilier reflux gastritis	47 (21.5)
Helicobacter pylori gastritis and bilier reflux gastritis	54 (24.8)
Ulcer	27 (12.4)
WBC median (min-max)	6830 (3670-15780)
ANC/ ALC median (min-max)	1.42 (0.28-9.40)
RBC mean±SD	5.0±0.43
HB mean±SD	13.97±1.38
HTC mean±SD	42.08±3.80
MCV mean±SD	84.12±4.33
Platelet mean±SD	294000±66000
MPV mean±SD	10.03±0.83

Variables with normal distribution were shown as mean±SD, and variables not with normal distribution as median (min-max). WBC: White blood cell, ANC/ALC: Absolute neutrophil count/ Absolute lymphocyte count, RBC: Red blood cell, HTC: hematocrit, MCV: Mean corpuscular volume, MPV: Mean platelet volume

When the groups were compared within themselves, no statistically significant difference was found between the rates of WBC, MPV and ANC/ALC ratio (**Table 2**).

Table 2. Comparison of hematological parameters between groups

n=218	*Helicobacter pylori* gastritis (n=117)	Bilier reflux gastritis (n=47)	*Helicobacter pylori* gastritis and Bilier reflux gastritis (n=54)	P value
WBC median (min-max)	6850 (4190-15780)	6520 (3670-13510)	7025 (4110-12600)	0.344
ANC/ALC median (min-max)	1.33 (0.28-8.45)	1.56 (0.54-8.02)	1.47 (0.44-9.40)	0.120
MPV mean±SD	9.97±0.82	10.16±0.81	10.06±0.88	0.376

One way ANOVA was performed for the variables with normal distribution, and Kruskal-Wallis tests were performed for variables not with normal distribution. Variables with normal distribution were shown as mean±SD, and variables not with normal distribution as median (min-max). WBC: White blood cell, ANC/ALC: Absolute neutrophil count/ Absolute lymphocyte count, MPV: Mean platelet volume, Statistically significant at $P \leq 0.05$.

When the patients in the Group 1 were classified as mild, moderate and severe according to the degree of disease, no statistically significant difference was found in hematological parameters (**Table 3**).

Table 3. Comparison of disease degree and hematological parameters of patients in Group 1

***Helicobacter pylori* gastritis (n=117)**	**Mild n=76**	**Moderate n=21**	**Severe n=20**	**P value**
WBC Median (min-max)	6885 (4190-15780)	7180 (4800-9700)	6590 (4680-9880)	0.722
ANC/ALC Median (min-max)	1.29 (0.28-8.45)	1.41 (0.78-2.69)	1.39 (0.49-3.71)	0.479
MPV mean±SD	9.98±0.79	9.80±0.80	10.08±0.96	0.547

One way ANOVA was performed for the variables with normal distribution, and Kruskal-Wallis tests were performed for variables not with normal distribution. WBC: White blood cell, ANC/ALC: Absolute neutrophil count/ Absolute lymphocyte count, MPV: Mean platelet volume, Statistically significant at P ≤0.05.

DISCUSSION

Dyspeptic symptoms in children, which include various gastrointestinal discomforts like pain, bloating, and nausea, are indeed common.[14] While functional issues are a leading cause, there are organic causes such as *H. pylori* infection and bile reflux gastritis that can also contribute. *H. pylori* infection is a bacterial infection that can lead to gastritis and ulcers in the stomach and small intestine.[14,15] It's a significant public health concern, particularly in areas with low socio-economic status and rural regions.[6,16,17] Bile reflux gastritis occurs when bile from the small intestine flows back into the stomach, leading to inflammation and irritation of the stomach lining. Poor eating habits can increase the risk of this condition.[7]

Diagnosing these conditions accurately is important for proper management. Histopathologic examination, which involves analyzing tissue samples under a microscope, is a reliable method for distinguishing between different causes of gastrointestinal diseases. However, this examination usually requires upper gastrointestinal endoscopy. Performing endoscopy in children can be challenging due to their discomfort and potential anxiety.[1-7] In summary, dyspeptic symptoms in children can stem from both functional and organic causes, including *H. pylori* infection and bile reflux gastritis. Accurate diagnosis often involves histopathologic examination through upper gastrointestinal endoscopy, which can be difficult to perform in children. Advances in medical technology and techniques may lead to less invasive methods for diagnosing these conditions in the future.

To our knowledge, this is the first study to evaluate the potential diagnostic value of MPV and ANC/ALC ratio parameters in differentiating pediatric patients with *H. pylori* gastritis and bile reflux gastritis.

Although studies examining the relationship between hematological parameters and *H. pylori* gastritis are rare, we have not found a study evaluating these parameters in patients with bile reflux gastritis. From this point of view, our study contributes to the literature.

In our study, hematological parameters were evaluated in the pediatric patient group who underwent gastroduodenoscopy. There was no statistically significant difference between ANC/ALC ratio and MPV values in all 3 groups. One of the few studies in the literature comparing MPV values in pediatric patients did not show a significant change in MPV values in patients with *H. pylori* gastritis.[16] Similarly, our study did not find a significant change in MPV values in children with gastritis, regardless of etiology.

In a study conducted by Sağlam et al.[17] no statistically significant difference was found between the group with and without *H. pylori* gastritis, between ANC/ALC ratio and MPV values. In a study by Melit et al.[18] no statistically significant difference was found between the ANC/ALC ratio values between the *H. pylori* gastritis group and the control group, similar to our results.

The study conducted by Jafarzadeh et al.[19] aimed to investigate the WBC and ANC/ALC ratio in adult patients with peptic ulcers infected with *Helicobacter pylori* compared to asymptomatic patients, and to analyze if there is a relationship between these parameters. Both *H. pylori* infected peptic ulcer patients and asymptomatic patients had significantly higher WBC compared to the control group. This suggests that the presence of *H. pylori* infection or peptic ulcer might lead to an elevated leukocyte response. In this study, the ANC/ALC ratio was found to be significantly higher in both *H. pylori* infected peptic ulcer patients and asymptomatic patients when compared to the control group. This suggests that the presence of *H. pylori* infection or peptic ulcer is associated with an increased ANC/ALC ratio, indicating higher inflammation levels. In our study, there was no control group, but it was found that WBC was higher in patients with bile reflux gastritis and *H. pylori* gastritis, although it was not statistically significant.

In the study of Şahin et al.[20] no relationship was found between ANC/ALC ratio and MPV values and childhood *H. pylori* infection, severity classification, or pre- and post-treatment status. In our study, no statistically significant difference was found between the ANC/ALC ratio and MPV values between groups.

Limitations of this study include the retrospective nature of the data with all cases collected from a single hospital and the low sample size.

CONCLUSION

ANC/ALC ratio and MPV can be easily calculated from routinely available data. ANC/ALC ratio can be an important measure of systemic inflammation because it is cost-effective and readily available. In this study, we showed that there was no difference between ANC/ALC ratio and MPV values in pediatric patients with bile reflux gastritis, until a new parameter is available, the use of upper gastrointestinal endoscopy, an invasive method to differentiate these diseases, will probably continue.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Sivas Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date:22.06.2022, Decision No: 2022-06/28).

Informed Consent: Because the study was designed retrospectively, no written informed consent from was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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REFERENCES

1. Tack J, Talley NJ. Functional dyspepsia--symptoms, definitions and validity of the Rome III criteria. *Nat Rev Gastroenterol Hepatol.* 2013;10(3):134-141.
2. Ford AC, Mahadeva S, Carbone MF, et al. Functional dyspepsia. *Lancet.* 2020;396(10263):1689-1702.
3. Vanheel H, Carbone F, Valvekens L, et al. Pathophysiological abnormalities in functional dyspepsia subgroups according to the Rome III criteria. *Am J Gastroenterol.* 2017;112(1):132-140.
4. Guarner J, Kalach N, Elitsur Y, Koletzko S. *Helicobacter pylori* diagnostic tests in children: review of the literature from 1999 to 2009. *Eur J Pediatr.* 2010;169(1):15-25.
5. Ortiz-Princz D, Villalta B, Urresterazu M, Serrano N, Cavazza M. Detection of *Helicobacter pylori* genes in Venezuelan children with recurrent abdominal pain: an infection to monitor closely. *Rev Soc Ven Microbiol.* 2013; 33 (1): 322-327
6. Ruggiero P. *Helicobacter pylori* and inflammation. *Curr Pharm Des.* 2010;16(38):4225-4236.
7. Shi X, Chen Z, Yang Y, Yan S. Bile reflux gastritis: insights into pathogenesis, relevant factors, carcinomatous risk, diagnosis, and management. *Gastroenterol Res Pract.* 2022;2022:2642551.
8. Basnayake C, Geeraerts A, Pauwels A, et al. Systematic review: duodenogastroesophageal (biliary) reflux prevalence, symptoms, oesophageal lesions and treatment. *Alimentary Pharmacology & Therapeutics.* 2021;54(6):755-778.
9. Futagami S, Yamawaki H, Agawa S, et al. New classification Rome IV functional dyspepsia and subtypes. *Transl Gastroenterol Hepatol.* 2018;3:70.
10. Nathan SD, Mehta J, Stauffer J, et al. Changes in neutrophil-lymphocyte or platelet-lymphocyte ratios and their associations with clinical outcomes in idiopathic pulmonary fibrosis. *J Clin Med.* 2021;10(7):1427.
11. Papa A, Emdin M, Passino C, Michelassi C, Battaglia D, Cocci F. Predictive value of elevated neutrophil lymphocyte ratio on cardiac mortality in patients with stable coronary artery disease. *Clin Chim Acta.* 2008;395:27-31.
12. Paliogiannis P, Fois AG, Sotgia S, et al. Neutrophil to lymphocyte ratio and clinical outcomes in COPD: Recent evidence and future perspectives. *Eur Respir Rev.* 2018;27(147):170113.
13. Shah B, Sha D, Xie D, et al. The relationship between diabetes, metabolic syndrome, and platelet activity as measured by mean platelet volume: the National Health and Nutrition Examination Survey, 1999-2004. *Diabetes Care.* 2012;35(5):1074-1078.
14. Jones MP, Guthrie-Lyons L, Sato YA, Talley NJ. Factors associated with placebo treatment response in functional dyspepsia clinical trials. *Am J Gastroenterol.* 2023;118(4):685-691.
15. Stanghellini V, Chan FKL, Hasler WL, et al. Gastroduodenal disorders. *Gastroenterology.* 2016;150(6):1380-92.
16. Agin M, Kayar Y, Dertli R. The relationship between mean platelet volume and platelet levels of children with *Helicobacter pylori* and gastritis. *Prz Gastroenterol.* 2019;14(3):198-201.
17. Sağlam NÖ, Civan HA. Impact of chronic *Helicobacter pylori* infection on inflammatory markers and hematological parameters. *Eur Rev Med Pharmacol Sci.* 2023;27(3):969-979.
18. Meliț LE, Mărginean MO, Mocan S, Mărginean CO. The usefulness of inflammatory biomarkers in diagnosing child and adolescent's gastritis: STROBE compliant article. *Medicine (Baltimore).* 2019;98(26):e16188.
19. Jafarzadeh A, Akbarpoor V, Nabizadeh M, Nemati M, Rezayati MT. Total leukocyte counts and neutrophil-lymphocyte count ratios among *Helicobacter pylori*-infected patients with peptic ulcers: independent of bacterial CagA status. *Southeast Asian J Trop Med Public Health.* 2013;44(1):82-88.
20. Sahin Y, Gubur O, Tekingunduz E. Relationship between the severity of *Helicobacter pylori* infection and neutrophil and lymphocyte ratio and mean platelet volume in children. *Arch Argent Pediatr.* 2020;118(3):e241-e245.